23 NICOTINE-INDUCED SUBMUCOSAL GLAND SECRETION AND AIRWAY SMOOTH MUSCLE CONTRACTION HAVE DIFFERENT MECHANISMS.

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We have demonstrated strong effects of nicotine on airway gland secretion and on airway smooth muscle contraction. These effects may be due to stimulation of nicotinic receptors in ganglia and along postganglionic nerves or to a direct effect of nicotine on receptors in the end organ. We studied these two possible mechanisms in 2 series of experiments, one on glands and one on airway smooth muscle.

Studies on glands: We mounted tracheal segments from 76 ferrets (37 M, 39 F), mean weight 915±314 g in Ussing chambers. We applied the radioactive precursor $Na_2{}^{35}SO_4$ to the submucosal side of tracheal segments and measured ^{35}S in secretions obtained from the luminal side. We studied nicotine-induced mucus secretion in the presence and absence of the neural blocker tetrodotoxin (TTX) using a concentration (10^{-5}M) that blocked the secretory effect of electric field stimulation completely. We also examined the inhibitory effect of atropine (10^{-7}-10^{-4}M) and of hexamethonium (10^{-9}-10^{-4}M) on nicotine-induced secretion.

Studies on airway smooth muscle: We performed similar studies on tracheal rings from 18 ferrets (10 M, 8 F), mean weight, 1216±511 g. Muscle studies were performed in the same medium and under the same conditions as secretion studies. Antagonists tested against nicotine-induced muscle contraction were tetrodotoxin (10^{-5}), hexamethonium (10^{-6} M, 10^{-5} M) and atropine (10^{-8} M, 10^{-7} M, 10^{-6} M).

While tetrodotoxin inhibited strongly or blocked, nicotine-induced muscle contraction tetrodotoxin did not reduce nicotine-induced mucus secretion significantly (477±61 vs. 342±74%, $p<0.2$, without vs. with TTX, n=15). While the dose of atropine that blocked nicotine-induced muscle contraction was exactly the same as the dose that blocked ACh-induced muscle contraction doses of atropine blocking nicotine-induced mucus secretion were three orders of magnitude (1000x) higher than those required to block ACh-induced mucus secretion. Thus, at these doses atropine acted nonspecifically as a nicotinic (as well as muscarinic) blocking agent. Only results with hexamethonium were comparable between the 2 studies in that the same concentration of hexamethonium inhibited (10^{-6} M) or blocked (10^{-5} M) nicotine-induced muscle contraction and nicotine-induced gland secretion. Thus both effects of nicotine, nicotine-induced muscle contraction and nicotine-induced gland secretion, were mediated by nicotinic receptors because they were blocked by the specific nicotinic receptor antagonist hexamethonium. However, only nicotine-induced muscle contraction was mediated by neural pathways and was therefore TTX sensitive and was blocked by concentrations of atropine causing specific muscarinic blockade. In contrast, nicotine-induced gland secretion was caused by a direct effect of nicotine on nicotinic receptors in the end organ. It was therefore not TTX sensitive and was not blocked by concentrations of atropine causing specific muscarinic ACh receptor blockade.

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